REMARKS

Claims 16-27 are pending. The claims are amended and new claims 22-27 are added to more particularly set forth the applicants' invention. In particular, new claims 26 and 27 are supported by paragraph 20 of the specification. The specification has been amended, as required by the Examiner, to set forth the number of a priority document, Brazilian application PI0102648-8. Neither the amendments nor the new claims constitute new matter.

The claims are rejected under 35 U.S.C. §112 and 35 U.S.C. §103(a). For reasons set forth below, the rejections should be removed and the claims should be deemed allowable.

1. Priority Information Is Inserted Into The Specification

The Examiner has noted that the full priority information had not been incorporated into the priority claim statement in the specification. Applicants have now amended the specification to provide said information.

Applicants are in the process of obtaining the requested certified copies of both Brazilian priority documents, which will be forwarded to the Examiner upon receipt. Applicants apologize for the delay.

2. The Subject Matter Of The Claims Is Fully Described

Claims 16-18 and 21 are rejected under 35 U.S.C. §112, first paragraph.

The Examiner states

> [that the claims contain] subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 16 and its dependent claims 17-18 and 21 are directed to a genus of agents from all sources and species (both synthetic and natural) that inhibit sialic acid mediated attachment of mycoplasma to cells that has not been adequately described in the specification.

The Examiner states that "[h]ere, the term 'agent' in claim 16 is merely defined by function . . .All applicant provides is two species namely antibiotics and neuraminidase/trans-sialidase enzymes which are insufficient to describe the structure of [the] entire genus."

Applicants have amended claim 16 and added new claim 23 to recite particular species that may be used according to the invention, such that the agent is an antibiotic or is selected from the group consisting of an enzyme having trans-sialidase activity and an enzyme having neuraminidase activity and combinations thereof, thereby obviating the basis for the rejection, which should be removed.

3. The Claims Are Enabled

Claims 16-21 are rejected under 35 U.S.C. §112, first paragraph,

> because the specification, while being enabling for methods of use of antibiotics and active neuraminidase/trans-sialidase enzymes from T. cruzi for inhibiting sialic-acid mediated mycoplasma attachment to cells in the subject, does not reasonably provide enablement for use of all agents from all sources and species (both natural and synthetic) for inhibiting or preventing mycoplasma infection.

The Examiner further states:

> With respect to claim 19, applicant is reminded even though [in] said claim the source of trans-sialidase is specified, Uemura et al. (EMBO J. 11(11), 3837-3834, 1992, cited in the IDS) teaches that many trans-sialidase genes from T. cruzi with structures very similar to SEQ ID NO:2, do not express [products] that exhibit activity (see abstract). Therefore, in the absence of a clear structural information about claimed enzyme the invention is subject to scope of enablement rejection.

Additionally, the Examiner has objected to use of the term "prevents" in claim 16, contending that "[a]ll the information and data provided in the disclosure indicated reduction or inhibition of mycoplasma infection and not its total prevention."

Applicants have amended claim 16 to delete "prevents." Applicants have also amended claim 16 and added new claim 23 to limit the agents which may be used according to the invention, such that the agent may be an antibiotic or may be selected from the group consisting of an enzyme having trans-sialidase activity and an enzyme having neuraminidase activity and combinations thereof.

As regards the Examiner's contention that the only *T. cruzi* trans-sialidase enabled has the sequence of SEQ ID NO:2, Applicants respectfully disagree. The reference cited by the Examiner, Uemura et al., while reporting that, of various genes having similar nucleic acid sequences, only some produce active enzymes, goes on to state:

> Chimeric protein constructs combining different portions of active and inactive genes identified a region of the gene necessary for enzymatic activity. Sequence analysis of this portion of the gene revealed a limited number of amino acid differences between the predicted active and inactive gene products.

Therefore, even based on Uemura, the skilled artisan would be able to distinguish between active and inactive genes. Further, it would be well within the capabilities of the

skilled artisan to, using standard laboratory tests, determine whether or not a given enzyme has trans-sialidase activity.

For all the foregoing reasons, the rejection of the claims should be withdrawn.

4. Claims 16 and 21 Are Not Obvious

Claims 16 and 21 are rejected under 35 U.S.C. §103(a) as obvious over Chandler et al., 1982, Infect. and Immun. 38(2):598-603 ("Chandler") in view of Feng et al., 1999, Mol. Cell. Biol. 19(12):7995-8002 ("Feng"). According to the Examiner

> Chandler teaches that *Mycoplasma pneumoniae* (*M. pneumoniae*) attachment to human intestinal carcinoma cultures (WiDr) occurs on neuraminidase sensitive, sialic acid containing glycoproteins (see page 598). Chandler also teaches a method of inhibiting mycoplasma binding to WiDr cells 'in vitro' or 'in situ', comprising preincubating said cells with sialoglyoproteins and gangliosides thereby saturating the mycoplasma surface proteins with sialate residues from said products before exposing WiDr receptor cells to mycoplasma (see Table 3). Chandler does not teach methods of treating undesirable cell proliferation associated with mycoplasma infection in a subject, utilizing agents that inhibit sialic-acid mediated attachment of mycoplasma to cells of the subject. Feng teaches that chronic infection by mycoplasma induces chromosomal instability as well as malignant transformation of mammalian cells (see page 7995). At the time the invention was made it would have been obvious to one or ordinary skill in the art to start with the 'in vitro' method of Chandler and administer the sialoglycoproteins or gangiolsides in humans in order to treat malignant transformation of mammalian cells such as colon, prostate, lung, etc. as taught by Feng. One of ordinary skill in the art is motivated in administering said sialoglyoproteins and gangliosides to patients because such products would reduce mycoplasma infection and its associated cell proliferation, in patients and have potential be used as drugs against a variety of cancers in humans and animals caused by mycoplasma infection. Finally, one or ordinary skill in the art has a reasonable expectation of success in administering such gangliosides or sialoglyoproteins (products) to mammalian subjects because said products are non-toxic and well established in terms of structure and organ targeting properties in the prior art, rendering the invention obvious.

Applicants respectfully assert that neither Chandler, nor Feng, nor their combination would render the claims obvious.

First, claim 16 has been amended (and claim 23 has been added) so that the agent administered to inhibit sialic-acid mediated attachment of mycoplasma can no longer be a ganglioside or sialoglyocprotein according to Chandler.

Second, even if the agent administered by Chandler would not be expected to have toxic effects, this is not tantamount to a reasonable expectation of success that the method presently claimed would be effective in treating undesirable cell proliferation.

Third, the addition of Feng to the disclosure of Chandler does not render the claims obvious because Feng leaves many questioned unanswered, among them the reasons behind the observation that "Heat-killed mycoplasmas or mycoplasmal membrane preparations alone could support continued growth of 32D cells in culture without IL-3 supplement for a substantial period of time." Feng did not provide any disclosure or suggestion that would link its observations to sialic-acid mediated attachment of mycoplasma. Moreover, even a teaching of mycoplasma-associated transformation/proliferation would provide no assurances that the claimed methods for inhibiting proliferation would work. Accordingly, the skilled artisan would not have been provided a reasonable expectation of success by Feng and Chandler.

Therefore, neither Chandler nor Feng nor their combination would render the claimed invention obvious, and the rejection should be removed.

5. Claims 17-19 Are Not Obvious

Claims 17-19 are rejected under 35 U.S.C. §103(a) as obvious over Chandler in view of Feng in view of Uemura. The Examiner states:

> At the time the invention was made, it would have been obvious to one of ordinary skill in the art to start with the method of Chandler in view of Feng and replace the inhibitor agent (namely sialoglycoproteins and gangliosides) with the active T. cruzi trans-sialidase of Uemura. One of ordinary skill in the art is motivated [in] replacing the sialoglycoproteins of Chandler in view of Fend with the enzyme of Uemura because said enzyme will successfully remove the sialate residues on the host cell receptors and will transfer them to some other miscellaneous proteins in the blood or tissues, such that said residues will be totally unavailable and inaccessible for mycoplasma binding and infection on the surface of host cells. One of ordinary skill in the art is motivated in replacing the inhibitor agent of Chandler in view of Feng with that of Uemura because T. cruzi trans-sialidase has both neuraminidase and trans-sialidase activities [in] a single enzyme and is expected to result in more inhibition that those provided by sialoglyroproteins of Chandler in view [of] Feng. Finally, one of ordinary skill in the art has a reasonable expectation of success in replacing the agents of Chandler in view of Fend with that of Uemura because once again methods of administering enzymes to mammalian organs are well established in the prior art, rendering the invention obvious.

Applicants respectfully disagree.

First, the fact that Chandler teaches preincubating cells with sialoglycoproteins and gangliosides to saturate mycoplasma surface proteins might at most motivate the skilled artisan to test whether transsialidase and/or neuraminidase might be effective in inhibiting attachment, but would not provide the requisite expectation of success as regards inhibiting cell proliferation.

Second, there would be no motivation to combine Uemura with the other references, as Uemura relates to a *T. cruzi* gene family expressing neuraminidase and

trans-sialidase activities and has no bearing on cell proliferation or mycoplasma whatsoever.

Third, the fact that enzymes are known to be administered to mammalian organs has no bearing on whether the methods of the invention would be successful in inhibiting undesirable cell proliferation.

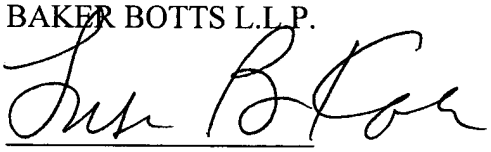
Finally, because Feng did not provide any disclosure or suggestion that would link its observations to sialic-acid mediated attachment of mycoplasma, it cannot create a reasonable expectation that the claimed enzymatic methods would successfully inhibit undesirable cell proliferation.

For all the foregoing reasons, neither Chandler, Feng, Uemura, nor any combination thereof, render the claimed invention obvious, so that the foregoing rejection should be removed.

6. Conclusion

For all the foregoing reasons, Applicants request that the rejections be removed and that the claims be allowed to issue.

Respectfully submitted,
BAKER BOTTS L.L.P.



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